Great Lakes Chemical Corporation

September 24, 2001

Dr. Scott Masten
Office of Chemical Nomination and Selection
NIEHS/NTP
P.O. Box 12233
Research Triangle Park, NC 27709

Re: Comments on the Substances Nominated to the NTP for Toxicological Studies and Testing Recommendations; FR Doc. 01-18481; 66 Fed. Reg. 38,717 (July 25, 2001)

Dear Dr. Masten:

Great Lakes Chemical Corporation (GLCC) is providing comments to the National Toxicology Program (NTP) on certain substances nominated to the NTP for toxicological studies and on the testing recommendations made by the Interagency Committee for Chemical Evaluation and Coordination (ICCEC) on May 8, 2001. *See* 66 Fed. Reg. 38,717 (July ˚25, 2001). GLCC commercially manufactures both Pentabromodiphenylether (Penta-BDPE, CAS 32534-81-9) and Octabromodiphenylether (Octa-BDPE, CAS 32536-52-0), both of which have been listed in the FR notice. While we do not isolate the three other specific polybrominated diphenylethers identified in the notice, these are present (in considerably different concentrations) in Penta-BDPE and/or Octa-BDPE.

Summary

GLCC encourages the NTP to place the three specific brominated diphenylether isomers in their future testing programs. Further, should NTP chose to proceed, we would be willing to provide support in the form of manpower, materials, analytical methods and other resources to assist in the conduct of studies on these isomers. These isomers in particular have been receiving a considerable amount of attention by environmental chemists and others. Information so far would indicate that exposures to the isomers are quite low and also diffuse in the environment. Based on the current manufacturing and use processes involving commercial Penta- and Octa-BDPE s it appears unlikely at this time that facilities currently producing or using the commercial products are the sources of 2,2'4,4'-Tetrabromodiphenyl ether [5436-43-1], 2,2',4,4',5-Pentabromodiphenyl ether [60348-60-9], and 2,2',4,4',5,5'-Hexabromodiphenyl ether [68631-49-2] in areas and biota which are geographically remote from these locations.

GLCC (either directly or as part of the American Chemistry Council s Brominated Flame Retardant Industry Panel) has conducted a number of in vitro and in vivo health effects studies using standardized protocols on the commercial penta-BDPE and octa-BDPE products. A list of the studies for each of these products can be found in Tables 1 and 2. Many of these studies were conducted for purposes of assessing the potential hazard to workers who may come into contact with these substances in the course of manufacturing or processing the substances. These existing studies may be useful to some extent for assessing the hazards of specific congeners potentially encountered by the general population through the environment, the types of studies recommended by the ICCEC are more relevant to the nature and modes of exposure for a low level, diffuse environmental contaminants.

Answers to Specific Requests for Public Comment

In the Federal Register Notice the NTP identified a number of areas for which they were seeking public comment from interested parties. GLCC wants to addresses these below. However, if there are other questions or further clarification needed, GLCC would be happy to meet and discuss these with NTP.

A. Status of On Going or Planned Studies:

GLCC does not have any in vitro or in vivo toxicological studies or physical/chemical property studies underway or planned at this time, either on the individual congeners or the commercial Octa- or Penta-BDPE products. GLCC has informed the EPA of our intent to cooperate with them in the Voluntary Children s Chemical Exposure Pilot Program (VCCEPP) by sponsoring both of the commercial products in the initial (Tier 1) portion. The details of what is involved in the commitment will not be detailed here, but the nature of the commitment is to do a screening level risk assessment using a core set of defined studies and exposure models. This commitment could require GLCC to conduct a study on reproductive toxicity (OECD 415/421). It most likely would involve the use of commercial Penta-BDPE. A decision on this will be made later this year.

GLCC, on behalf of the industrial consortium, ACC-BFRIP recently had discussions with Dr. Prasada Kodavanti, who is working with the USEPA in Research Triangle Park, NC. He has requested small quantities of several commercial brominated diphenyl ether products and 2,2 4,4 -tetraBDPE. We were told that the samples are to be used in a study that will look at mechanisms for neurotoxicity among a number of different compounds.

B. Production levels and Use Patterns

As indicated previously, GLCC does not manufacture for commercial purposes any of the individual isomers identified in the FR notice. The Bromine Science and Environment Forum (BSEF) have compiled approximate volumes for the commercial Penta and Octa-BDPE in the North America for the 1999 calendar year:

Octa-BDE (OBDPO) 1,375 metric tons
Penta-BDE (PBDPO8,290 metric tons

Octa-BDPE is used almost exclusively as an additive flame retardant in thermoplastic ABS type of polymers, commonly used in making electronic and electrical equipment housings more resistant to ignition from internal and external ignition sources. It is particularly well suited for this application because it will melt and be well incorporated into the polymer structure at ABS processing temperatures. Penta-BDPE is most commonly found in flame retarded flexible polyurethane foam. Flame retarded polyurethane foam is found in upholstered furniture, transportation products or other applications covered by state or federal flammability standards for institutional, commercial or consumer products. Historic uses around the world have found it to be used in the oil industry as a material used in offshore oil fields and as a component of ignition resistant hydraulic fluids. GLCC is not aware of any uses in these applications for many years.

C. Human Exposure/Environmental Occurrence

The number of workers involved in manufacturing these two substances in the US is quite small (exact numbers are considered proprietary, but are well below 100). Manufacturing occurs at our manufacturing operations in Southern Arkansas. Releases to the environment were reported previously to the OECD as part of our industry s voluntary product stewardship commitment. In 1998 releases of Octa-BDPE were estimated to be ~5000 pounds/year, all to the air. Releases of Penta-BDPE were estimated at 22,000 lbs., all to a secure, offsite landfill.

Reports in the scientific literature indicate that the three congeners of interest to the ICCEC have been found in low concentrations in freshwater and marine life and also in human breast milk. There have also been reports of finding low (pg/m3) concentrations of certain lower brominated DPE s (predominantly 2,2,4,4-tetra and 2,2,4,4,5-penta- bromodiphenylethers in the air around the Great Lakes. Highest levels were near Chicago (3-year average of 33 pg/m3 as 2,2,4,4-tetrabromodiphenylether).

Based on existing health effects data and current exposures, there appears to be a considerable margin of safety (MOS) between the concentrations being found and the effect concentrations seen in the available studies. For example, in a recently completed risk assessment of Penta-BDPE, European Union estimated a MOS of between 12,000 and 84,000 for infants exposed to Penta-BDPE at concentrations in the range of 3 ng/g of lipid (a concentration believed to be at the extreme high end of the data set).

Conclusion

The three brominated diphenyl ether isomers recommended for study by the ICCEP are worth further evaluation by the NTP. These substances are not produced or used for any commercial purpose and their presence in the environment represents a diffuse historic source, not likely to be associated with the current manufacturing or use of the commercial Penta- or Octa-BDPE s. The commercially available compounds have been reasonably well studied and further studies are being considered under the VCCEPP. However, the presence of the 2,2 4,4 - tetrabromoDPE (and to a lesser degree the 2,2 ,4,4 ,5 and 2,2 ,4,4 ,5,5 species) in a variety of environmental compartments and in breast milk provides the NTP an opportunity to provide important data on the effects at environmentally relevant concentrations. Data on the commercial products, while helpful in assessment of hazard to human health, will not address all the data needs recommended by the ICCEP. Without NTP involvement, it is unlikely that studies on carcinogenicity, neurotoxicity and other higher tiered studies would be performed on these isomers.

Sincerely,

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Table 1
OBDPO Toxicology Summary.

TEST	RESULTS
Water Solubility+	< 1 ug/L
Vapor Pressure+	6.59 x 10-6 Pa
Octanol/Water Partition Coefficient+	6.29
Oral LD50	> 28,000 mg/kg
Dermal LD50	> 2,000 mg/kg
Inhalation LC50	> 50 mg/L
Eye Irritation	Not an irritant
Skin Irritation	Not an irritant
Ames+	Not mutagenic
Sister Chromatid Exchange	Did not induce
Unscheduled DNA Synthesis	Did not induce
Chromosome Aberration	Did not induce
Guinea Pig Skin Sensitization+	Did not induce
28 Day Rat Oral (Diet)	Hepatic centrilobular hypertrophy @ 100, 1,000, 10,000 ppm diet:, scattered necrosis @ 10,000 ppm (~1,000 mg/kg/d); Liver wt increased.
90 Day Rat Oral (Diet)	Effects consistent with above @ 100, 1,000, 10,000 ppm diet/d.
14 Day Rat Inhalation; 8 hr/d	Hepatocytomegally & degeneration at ≥ 12 mg/m3; NOEL = 1.2 mg/m3.
90 Day Rat Inhalation; 6 hr/d 5 d/wk+	Hepatic centrilobular hypertrophy @ 15 & 200 mg/m3; Liver wt increased @ 200 mg/m3; NOEL = 1.0 mg/m3; NOAEL = 15 mg/m3.
Rat Developmental (Day 6-15 of Gestation)	Developmental toxicant NOEL = 25 mg/kg/d (maternal); 2.5 mg/kg (fetal).
Rabbit Developmental (Day 7-19 Gestation)	Not a developmental toxicant NOEL = 5 mg/kg/d (Slight fetotoxicity @ maternally toxic dose).

+Studies Performed under Good Laboratory Practices using the current commercial product.

Table 2.
PeBDPO Toxicology Summary.

TEST	RESULTS
Water Solubility+	13.3 ug/L (Sum for Commercial Product); 2.4 ug/L (2,2 ,4,4 ,5- PeBDPO); 10.9 ug/L (2,2 ,4,4 -TeBDPO)
Vapor Pressure+	4.69 x 10^{-5} Pa
Octanol /Water Partition Coefficient+	6.58
Oral LD50	7,400 or 5,800 mg/kg in male or female Wistar rats, respectively
Dermal LD50	> 2,000 mg/kg
Inhalation LD50	> 200 mg/L
Eye Irritation	Slight irritation
Skin Irritation	Not an irritant
Ames	Not mutagenic
Chromosome Aberration+	Did not induce aberrations
Guinea Pig Skin Sensitization+	Did not induce
28 Day Rat Oral (Diet)	Hepatic centrilobular hypertrophy @ 100 & 1000 ppm; Thyroid hyperplasia & increased liver wt @ 1,000 ppm; NOEL < 100 ppm (< ~10 mg/kg/d).
30 Day Rat Oral (Diet)	NOEL = 1 mg/kg/d (highest dose tested).
28 Day Rat Oral (Gavage)	Hepatic hypertrophy; Liver wt increased @ 250 mg/kg/d; NOEL not stated.
90 Day Rat Oral (Diet)	Hepatocytomegally @ d 28 & 90 @ 2, 10 or 100 mg/kg/d (except in 2 mg/kg/d females); Thyroid hyperplasia; T4 decreased @ 10 & 100 mg/kg/d @ d 28 but not @ d 90; Liver wt increased @ 100 mg/kg/d; NOEL < 2 mg/kg/d.
Rat Developmental	Not developmental toxicant @ 200 mg/kg/d (highest dose tested). NOEL = 10 mg/kg/d (maternal). NOEL = 100 mg/kg/d (fetal).
In Vitro Dermal Absorbtion in Rat and Human Skin (using 2,2 4,4 -TeBDPE)	<2% of applied dose absorbed (human), <15% absorbed (rat)

+Studies Performed according to Good Laboratory Practices using the current commercial product.